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| 10/673,000            | 09/26/2003  | Anne Skaja Robinson  | UOD-154US1          | 9773             |
| 6646/ 7590 06/11/2008 |             |                      |                     |                  |
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

### Office Action Summary

**Application No.**

10/673,000

**Applicant(s)**

ROBINSON ET AL.

**Examiner**

Amber D. Steele

**Art Unit**

1639

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 25 March 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-18 is/are pending in the application.
- 4a) Of the above claim(s) 13-18 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-12 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 03/03/04 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/06)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_

## **DETAILED ACTION**

### ***Status of the Claims***

1. The amendment to the claims received on November 2, 2006 amended claims 3, 5, 8, 11, 14, and 17.

The amendment to the claims received on October 12, 2007 amended claims 1 and 7 and added new claims 19-20.

The amendment to the claims received on March 25, 2008 amended claims 1 and 7 and canceled claims 19-20.

Claims 1-18 are currently pending.

Claims 1-12 are currently under consideration.

### ***Election/Restrictions***

2. Claims 1-6 are linking claims. Applicants elected Group I (Claims 7-12) in the reply filed on March 28, 2006 without traverse. Thus, claims 13-18 are withdrawn from consideration as being drawn to a non-elected invention.

### ***Priority***

3. The present application claims status as a divisional of 09/695,762 filed October 25, 2000, which claims benefit to provisional application 60/161,035 filed October 25, 1999.

### ***Invention as Claimed***

4. A method for recovering native protein from a sample comprising protein aggregates, said method comprising the steps of: (a) obtaining a sample comprising protein aggregates wherein the sample is substantially free of a denaturing agent; (b) subjecting the sample of step (a) to elevated hydrostatic pressure, whereby a portion of protein dissociates from said protein

aggregates; c) returning the sample of step (b) to ambient pressure without repeatedly cycling the sample between the elevated and the ambient pressures, whereby a portion of the dissociated protein refolds to native protein and variations thereof.

#### **Withdrawn Rejections**

5. The rejection of claims 1-12 and 19-20 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement regarding new matter is withdrawn in view of the claim amendments received on March 25, 2008.

6. Claims 1-12 are rejected under 35 U.S.C. 102(e) as being anticipated by Litt et al. U.S. Patent 6,635,469 (effective filing date of July 2, 1996).

#### **New Rejections Necessitated by Amendment**

##### ***Claim Rejections - 35 USC § 102***

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 1-12 are rejected under 35 U.S.C. 102(a) as being anticipated by Foguel et al. (i.e. by another due to Pedro Caetano de Sousa, Jr.) Biotechnology and Bioengineering 63(5): 552-558, 1999 (provided by applicants in the IDS).

For present claims 1-12, Foguel et al. teach methods for recovering native protein from a sample comprising protein aggregates comprising (a) obtaining a sample comprising protein

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aggregates and being substantially free of a denaturing agent, (b) subjecting the sample to elevated hydrostatic pressure, and (c) returning the sample to ambient pressure without repeatedly cycling the sample between the elevated and the ambient pressures (please refer to the entire reference particularly the abstract; pages 553 and 556; Figures 3-4). In addition, Foguel et al. teach inclusion bodies and chaotropic agents (please refer to the abstract; page 552-553).

Therefore, the presently claimed invention is anticipated by the teachings of Foguel et al.

9. Claims 1, 3, 7, and 8 are rejected under 35 U.S.C. 102(b) as being anticipated by Silva et al. Anomalous Pressure Dissociation of Large Protein Aggregates The Journal of Biological Chemistry 264(27): 15863-15868, 1989.

For present claims 1, 3, 7, and 8, Silva et al. teach methods of recovering native protein from a sample comprising protein aggregates comprising (a) obtaining a sample comprising protein aggregates which is free of denaturing agent, (b) subjecting the sample to elevated hydrostatic pressure causing dissociation, and (c) returning the sample to ambient pressure without repeated cycles (please refer to the entire reference particularly the abstract; pages 15863, 15865, 15866; Figures 2-3 and 6-9).

Therefore, the presently claimed invention is anticipated by the teachings of Silva et al.

#### ***Claim Rejections - 35 USC § 103***

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

11. Claims 1-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Litt et al. U.S. Patent 6,635,469 (effective filing date of July 2, 1996) and Silva et al. Anomalous Pressure Dissociation of Large Protein Aggregates *The Journal of Biological Chemistry* 264(27): 15863-15868, 1989.

For present claims 1 and 7, Litt et al. teach methods of recovering properly folded proteins from a sample comprising protein aggregates comprising (a) obtaining a sample comprising protein aggregates (i.e. including protein folding intermediates) without any urea or other reducing agents, (b) subjecting the sample to elevated hydrostatic pressure in order to partially dissociate proteins from aggregates, and (c) returning the sample to ambient pressure to allow refolding of the protein (please refer to the entire specification particularly columns 3-4, 6-12, and 15-20 and Examples). Litt et al. specifically teach that chaotropic agents are optional and that non-chaotropic agents may be utilized (please refer to the entire specification particularly column 4, lines 35-49; column 7, lines 27-40; column 8, lines 20-32; column 15, lines 51-67; column 16, lines 1-17; column 17, lines 45-67 and column 18, lines 1-31; column 19, lines 60-67; column 20, lines 1-5). In a preferred embodiment, Litt et al. does teach cycling between high pressure and ambient pressure in order to obtain the lowest energy state conformation (i.e. no partial folding, secondary structures, tertiary structures, etc.). Please refer to column 8, lines 50-58; Figure 5; column 9, lines 15-36; column 17, lines 45-67; and column 18, lines 1-31.

For present claims 2, 6, 9, and 12, Litt et al. teach aggregates comprising inclusion bodies (please refer to the entire specification particularly column 17, lines 45-67 and column 18, lines 1-31).

For present claim 3, 5, 8, and 11, Litt et al. teach partial denaturing or reversible dissociation (please refer to the entire specification particularly column 9, lines 15-36; column 11, lines 46-56; column 15, lines 51-67; column 16, lines 1-17).

For present claims 4 and 10, Litt et al. teach that chaotropic agents are optional, non-chaotropic agents can be utilized, or temperature can be utilized instead (i.e. chaotropic agent in amount insufficient to denature protein at ambient pressure; please refer to the entire specification particularly column 4, lines 35-49; column 7, lines 27-40; column 8, lines 20-32; column 15, lines 51-67; column 16, lines 1-17; column 17, lines 45-67 and column 18, lines 1-31; column 19, lines 60-67; column 20, lines 1-5).

However, Litt et al. teaches cycling between high pressure and ambient pressure in order to obtain the lowest energy state conformation (i.e. no partial folding, secondary structures, tertiary structures, etc.).

For present claims 1, 3, 7, and 8, Silva et al. teach methods of recovering native protein from a sample comprising protein aggregates comprising (a) obtaining a sample comprising protein aggregates which is free of denaturing agent, (b) subjecting the sample to elevated hydrostatic pressure causing dissociation, and (c) returning the sample to ambient pressure without repeated cycles (please refer to the entire reference particularly the abstract; pages 15863, 15865, 15866; Figures 2-3 and 6-9).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to modify the methods of cycling between ambient and high pressure for dissociation of aggregates taught by Litt et al. with the non-cycling methods for dissociation of aggregates taught by Silva et al.

One having ordinary skill in the art would have been motivated to do this because Silva et al. teach that hydrostatic pressure can be utilized without cycling to dissociate large protein aggregates without altering secondary or tertiary structures of the proteins (please refer to page 15863, right column). Thus, aggregates can be dissociated without completely denaturing the protein of interest (i.e. more conducive to subsequent assays; e.g. binding, function, etc.).

One of ordinary skill in the art would have had a reasonable expectation of success in the modification of the methods of cycling between ambient and high pressure for dissociation of aggregates taught by Litt et al. with the non-cycling methods for dissociation of aggregates taught by Silva et al. because of the data provided by Silva et al. (please refer to Figures 1-9).

Therefore, the modification of the methods of cycling between ambient and high pressure for dissociation of aggregates taught by Litt et al. with the non-cycling methods for dissociation of aggregates taught by Silva et al. render the instant claims *prima facie* obvious.

### ***Conclusion***

12. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,



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however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

***Future Communications***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amber D. Steele whose telephone number is 571-272-5538. The examiner can normally be reached on Monday through Friday 9:00AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James (Doug) Schultz can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

ADS  
May 30, 2008

/Jon D. Epperson/  
Primary Examiner, AU 1639